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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,997	12/24/2003	Yukio Nihei	245553US0CONT	9427

22850 7590 08/22/2006

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/743,997	NIHEI ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-19,21-26 and 28-49* is/are pending in the application.

4a) Of the above claim(s) *16-19,21-26 and 28* is/are withdrawn from consideration.

5)☒ Claim(s) *29, 33 and 34* is/are allowed.

6)☒ Claim(s) *1, 3-15, 30-32, and 35-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 17, 2006 has been entered.

Status of Claims

Claims 1, 3-15, 29-49 are pending and are examined.

Claims 2, 20 and 27 are cancelled.

Claims 16-19, 21-26 and 28 are withdrawn.

Claim 29, 33 and 34 are allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30, 32, 35, 36-39-42, 44-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for AC 7700 ((Z)-N-[2-methoxy-5[2(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide combine with dexamethasone to treat a representation of tumors does not reasonably provide enablement for a wide

representation of tubulin polymerization-inhibitory active substances with dexamethasone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

In the instant case, applicants are claiming a method of treatment of tumors comprising the administration of an effective amount of one or more tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone. (see claim 30)

Nature of the invention.

The nature of the invention is method of treatment of tumors comprising the administration of an effective amount of one or more tubulin polymerization – inhibitory active substance having anti-tumor activity combined with dexamethasone.

(see claim 30). As stated, however, claim 30 recite that any of one or more tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone is/are intended.

Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is found on pages 22-27, however, no example is shown how more than one tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone was carried out.

Existence of working examples.

As discussed above, Applicant's limited working example does not enable one of skill in the art to use more than one tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone for the treatment of tumors as encompassed by the instant invention.

Breadth of claims.

Claim 30 is extremely broad due to the vast number of possible compounds of tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone encompassed by the instant invention.

II. Claims 30, 32, 35, 36-39-42, 44-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for AC 7700 ((Z)-N-[2-methoxy-5[2(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide combine with dexamethasone for the treatment of malignant fibrous histiocytoma does not reasonably provide enablement for a wide representation of treatment of a large/wide representation of tumors with one or more tubulin polymerization-inhibitory active substances with dexamethasone. The specification does not enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

In the instant case, applicants are claiming a method of treatment of tumors comprising the administration of an effective amount of one or more tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone. (see claim 30)

Nature of the invention.

The nature of the invention is method of treatment of tumors comprising the administration of an effective amount of one or more tubulin polymerization – inhibitory active substance having anti-tumor activity combined with dexamethasone. (see claim 30). As stated, however, claims 30 and 39 recite that any of one or more

tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone for the treatment of any variation of tumor is/are intended.

Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is found on pages 22-27, however, no example is shown how more than one tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone on a representative variation of tumor was carried out.

Existence of working examples.

As discussed above, Applicant's limited working example does not enable one of skill in the art to use more than one tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone for the treatment of tumors as encompassed by the instant invention.

Breadth of claims.

Claims 30 and 39 are extremely broad due to the vast number of possible compounds of tubulin polymerization –inhibitory active substance having anti-tumor activity combined with dexamethasone to treat a wide variation of tumors encompassed by the instant invention.

III. Claims 30-32, 35-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" one or more tubulin polymerization-inhibitory active substance, an ester of dexamethasone (as in claims 30, 32, 39 and 44)

or derivatives of combretastatines, vinca alkaloids, dolastatins etc (as in claims 31, 43 and 49) means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]."

In other words, the Applicant has not described with sufficient clarity a what these derivatives of the various compounds discussed above contemplated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 1, 3-4, 6-8,10, 12-15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Petit US 5,561,122 or Cushman et al. J. Med. Chem in view of Fex et al. US 3,732,260.

The rejection in the office action mailed 12/21/05 remain rejected as stated in the office action of record.

II. Claims 1, 3-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hori et al. Med. Sci Monit in view of Fex et al. US 3,732,260.

Hori et al. teach AC 7700 ((Z)-N-[2-methoxy-5[2(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide) (see abstract) as an anti –cancer agent with anti-cancer activity as in claim 1 in part and 11 wherein the unit dosage of the AC 7700 is 10 mg/kg in a unit dosage (see page 28 highlighted) as in claim 14. 10 mg/kg is within the claim limitation for example if weight of the patient is 50 then the unit dose is 500 mg.

Fex et al. teach administration of steroidal compounds with other pharmaceutically active agents (see col. 4 lines 33+) as in claim 1, wherein the unit dose of the steroid is 10-100 mg (see col. lines 33-61). Also Fex teaches that the compounds (steroids) can be used with treatment with anti-cancer agent thus including any anti-cancer agent thereof (see col. 2 lines 15+).

Although the Hori et al. did not teach using an adjuvant therapy, one skilled in the art would have being motivated to combine the teachings of Hori et al. with that of Fex et al. to result in the claim invention of the instant subject matter.

Claim 29 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ardin H. Marschel 8/18/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

SVG
8/15/06